

Application No. 09/862,571
Amendment dated 02/06/06
Reply to Office Action of July 25, 2005

Expedited Procedure under 37 C.F.R. § 1.116
Examining Group 1631
Docket No.: AFMX-P02-038

AMENDMENTS TO THE CLAIMS

1. (Previously Presented) A method for reducing non-specific binding of a molecule to an oligonucleotide array comprising a plurality of oligonucleotides on a surface of a solid support, wherein said surface has a plurality of designated regions and a plurality of protected regions, each of said plurality of protected regions having a protecting group thereon, said method comprising:
 - a) producing said plurality of oligonucleotides at each of said designated regions, each of said plurality of oligonucleotides having a terminal protecting group; and
 - b) replacing with a negatively charged phosphate residue, at least one of:
 - i) the protecting groups on each of said plurality of oligonucleotides produced in step a), and
 - ii) the protecting groups on each of said plurality of protected regions; whereby non-specific binding of said molecule is reduced.
2. (Original) The method according to Claim 1, wherein said solid support comprises polymerized Langmuir Blodgett film, functionalized glass, germanium, silicon, polymers, (poly)tetrafluoroethylene, polystyrene, gallium arsenide, metal oxide films, and combinations thereof.
3. (Previously Presented) The method according to Claim 1, wherein said step a) of producing said plurality of oligonucleotides comprises:
 - 1) attaching to each of said designated regions an independently selected linker monomer having a photolabile protecting group;
 - 2) attaching an independently selected nucleotide monomer having a photolabile protecting group to each of said attached linker monomers using light directed methods to produce a plurality of attached monomers each having a terminal photolabile protecting group;
 - 3) attaching an independently selected nucleotide monomer having a photolabile protecting group to each of said attached monomers using light directed methods

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- to produce a plurality of oligonucleotides each having a terminal photolabile protecting group; and
- 4) repeating step 3) from 0 to 119 times, to attach subsequent nucleotide monomers to each of said oligonucleotides produced in step 3) to produce a plurality of oligonucleotides having a terminal photolabile protecting group.
4. (Withdrawn) The method according to Claim 1, wherein said step *a*) of producing said plurality of oligonucleotides comprises:
- 1) attaching to each of said designated regions an independently selected linker monomer having a chemically-removable protecting group;
 - 2) replacing each of said chemically-removable protecting groups on each of said attached linker monomers with a photolabile protecting group;
 - 3) attaching an independently selected nucleotide monomer having a chemically-removable protecting group to each of said attached linker monomers using light-directed methods to produce a plurality of attached monomers each having a terminal chemically-removable protecting group;
 - 4) replacing each of said chemically-removable protecting groups on each of said attached monomers with a photolabile protecting group;
 - 5) attaching an independently selected nucleotide monomer having a chemically-removable protecting group to each of said attached monomers using light-directed methods to produce a plurality of oligonucleotides each having a terminal chemically-removable protecting group;
 - 6) replacing each of said chemically-removable protecting groups on each of said oligonucleotides produced in step 5) with a photolabile protecting group; and
 - 7) repeating steps 5) and 6) from 0 to 119 times, to attach subsequent nucleotide monomers to each of said oligonucleotides produced in step 5) to produce said plurality of oligonucleotides having a terminal chemically-removable protecting group.
5. (Withdrawn) The method according to Claim 1, wherein said step *a*) of producing said plurality of oligonucleotides comprises:

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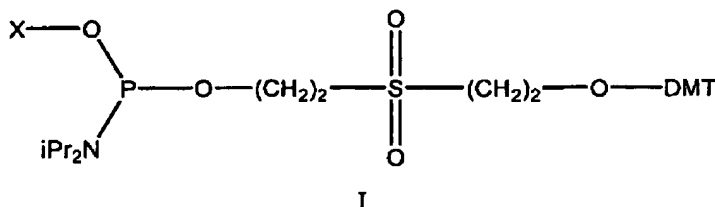
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- 1) attaching to each of said designated regions an independently selected linker monomer having a chemically-removable protecting group;
 - 2) forming an activation layer on said designated regions and said protected regions, said activation layer comprising:
 - i) a photoactive agent, said photoactive agent producing a catalyst when irradiated, and
 - ii) an autocatalytic agent, said autocatalytic agent generating a product that removes said chemically-removable protecting group when said autocatalytic agent is activated by said catalyst;
 - 3) irradiating a portion of said activation layer overlying said designated regions to remove said chemically-removable protecting group on said linker monomer;
 - 4) attaching an independently selected nucleotide monomer having a chemically-removable protecting group to each of said attached linker monomers, to produce a plurality of attached monomers each having a terminal chemically-removable protecting group;
 - 5) irradiating a portion of said activation layer overlying said designated regions to remove said chemically-removable protecting group on said attached monomers;
 - 6) attaching an independently selected nucleotide monomer having a chemically-removable protecting group to each of said attached monomers, to produce a plurality of oligonucleotides each having a terminal chemically-removable protecting group;
 - 7) irradiating a portion of said activation layer overlying said designated regions to remove said chemically-removable protecting group on said oligonucleotides produced in step 6); and
 - 8) repeating steps 6) and 7) from 0 to 119 times, to attach subsequent nucleotide monomers to each of said oligonucleotides produced in step 6) to produce said plurality of oligonucleotides having a terminal chemically-removable protecting group.
6. (Previously Presented) The method according to Claim 1, wherein said step *b*) of replacing comprises:

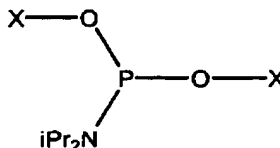
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- 1) exposing at least one of: *i*) each of said plurality of oligonucleotides and *ii*) each of said plurality of protected regions, to an activator to remove the protecting groups, to produce activated sites; and
 - 2) reacting said activated sites with one or more compounds that result in a negatively charged phosphate residue becoming bound to at least one of *i*) each of said plurality of oligonucleotides and *ii*) each of said plurality of protected regions.
7. (Original) The method according to Claim 6, wherein said protecting group is a photolabile protecting group and said activator is selected from the group consisting of ion beams, electron beams, gamma rays, x-rays, ultra-violet radiation, light, infra-red radiation, microwaves, electric currents, radiowaves, and combinations thereof.
8. (Withdrawn) The method according to Claim 6, wherein said protecting group is a chemically-removable protecting group and said activator is selected from the group consisting of acids, bases, oxidants, and reductants.
9. (Currently Amended) The method according to Claim 6, wherein said step 2) of reacting said activated sites with a compound comprises reacting each of said activated sites with a compound selected from the group consisting of Formula I:



and Formula II:



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II

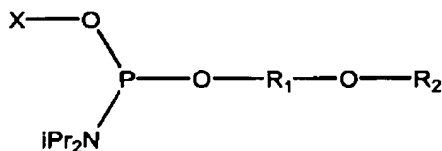
wherein:

DMT is a dimethoxy trityl protecting group;
 each X is a base-removable protecting group; and
 iPr₂N is diisopropyl amino protecting group,

thereby forming a phosphite;

removing the protecting groups and oxidizing the phosphite to a phosphate, said
removing and oxidizing resulting in a negatively-charged phosphate group.

10. (Withdrawn) The method according to Claim 1, wherein said step *b*) of replacing comprises:
 - 1) exposing at least one of: *i*) each of said plurality of oligonucleotides and *ii*) each of said plurality of protected regions, to an activator to remove the protecting groups to produce activated sites;
 - 2) reacting said activated sites with a monomer having a negatively charged phosphate unit and a protecting group, whereby said monomer is covalently bound to at least one of *i*) each of said plurality of oligonucleotides and *ii*) each of said plurality of protected regions; and
 - 3) repeating steps 1) and 2) from 1 to 20 times to produce a polyanion chain of negatively charged phosphate units on at least one of *i*) each of said plurality of oligonucleotides and *ii*) each of said plurality of protected regions.
11. (Withdrawn and Currently Amended) The method according to Claim 10, wherein said step 2) comprises reacting with a monomer of Formula III:



III

wherein:

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R_1 is selected from the group consisting of a nucleoside moiety, a deoxyribose moiety, C_{1-8} alkylene, and $-(CH_2CH_2O)_m-$ wherein m is an integer from 1 to 8;

R_2 is a protecting group selected from the group consisting of a dimethoxy trityl protecting group and a MeNPOC protecting group;

X is a base-removable protecting group; and

iPr_2N is diisopropyl amino protecting group,

thereby forming a phosphite;

removing the protecting groups and oxidizing the phosphite to a phosphate, said

removing and oxidizing resulting in a negatively-charged phosphate group.

12. (Original) The method according to Claim 1, wherein said step *b*) of replacing comprises replacing both *i*) the protecting groups on each of said plurality of oligonucleotides produced in step *a*), and *ii*) the protecting groups on each of said plurality of protected regions.

13-42. Canceled.

43. (New) The method according to Claim 1, wherein non-specific binding of a nucleic acid polymer to an oligonucleotide array is reduced.

44. (New) The method according to Claim 43, wherein the nucleic acid molecule is an oligonucleotide.